Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Chin ET, Leidner D, Zhang Y, et al. Effectiveness of the mRNA-1273 vaccine during a SARS-CoV-2 delta outbreak in a prison. N Engl J Med. DOI: 10.1056/NEJMc2114089

SUPPLEMENTARY APPENDIX

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1 Study design

1.1 Study setting

Sierra Conservation Center (SCC) is a low-to-medium security prison for men located in Tuolumne County, California. SCC is separated into three facilities: two facilities with dormitory housing and one facility with celled housing. SCC also manages 16 Conservation Camps, which are sited in rural or wilderness areas for fire suppression. SCC has a design capacity of 3,404,¹ and was 94.6% occupied with 3,221 residents on July 16, 2021. Between July 1 and August 31, 2021, 1,219 staff worked at SCC, including 688 custody and 146 healthcare workers. Among all staff, 490 (40.2%) were vaccinated with at least one dose prior to July 16, 2021; the proportion vaccinated was higher among healthcare staff (64.4%) and lower among custody staff (32.0%). Over the study period, there were 39 confirmed infections among all staff, 28 of which were detected among custody staff.

Detailed SARS-CoV-2 testing information came from a multilayered resident testing program that included risk-based routine testing, surveillance testing, and testing in response to detected outbreaks.² In response to detection of the first resident case on July 16, 2021, 95.6% of all residents present in that facility on that night were tested within 7 days. Residents who had close contact or a potential exposure risk to confirmed cases were placed in quarantine. Serial re-testing was conducted on day 5 and between days 12 and 14 for quarantined residents (Figures S1 and S2).

Prior to the outbreak, residents were served meals in dining halls with seating separated by housing unit. The two facilities with dormitories shared the same dining facility. Residents in quarantine ate meals in their rooms. During the outbreak, SCC implemented infection control measures including but not limited to restrictions on resident movement, quarantine, isolation, Covid-19 response testing, cleaning of areas of potential transmission, suspension of in-person and family visiting, staffing of essential personnel only, random audits of masking compliance, closing outdoor telephone booths, and programming with reduced group sizes, modified hours, staggered schedules, or in non-traditional spaces to allow for physical distancing.

1.2 Definition of the analytic cohort

Daily data extracts provided by the California Department of Corrections and Rehabilitation (CDCR) included a unique pseudo-identifier that allowed us to follow individual residents over time.

Residents were included in the analytic cohort if they:

- were incarcerated in the Sierra Conservation Center (SCC) on July 16, 2021
- were either unvaccinated or fully vaccinated during the entire study period
- resided in a housing unit with at least one detected case

1.3 Study period

The study period began on July 16, 2021, the first date a case was detected in SCC following a period of containment (no detected infections) since April 23, 2021. The end date for the study period was August 15, 2021.

1.4 Variables

<u>Prior SARS-CoV-2 infection</u>. The data included Covid-19 testing information. CDCR has undertaken extensive testing of residents for SARS-CoV-2 since April 2020, using real-time PCR and antigen tests. We defined a prior SARS-CoV-2 infection as having had at least one positive test in CDCR's clinical records prior to the beginning of the study period (Figure S3). Residents with positive SARS-CoV-2 tests within the 90 days prior to the beginning of the study period were excluded because of difficulties discerning positive tests from breakthrough infections or past infections.

¹ California Department of Corrections and Rehabilitation. Weekly Report of Population. July 14, 2021. https://www.cdcr.ca.gov/research/wp-content/uploads/sites/174/2021/07/Tpop1d210714.pdf

² California Correctional Health Care Services. COVID-19 Testing Definitions and Strategies. COVID-19 and Seasonal Influenza: Interim Guidance for Health Care and Public Health Providers. Revised: February 19, 2021.

<u>Race or ethnic group</u>. We grouped race and ethnicity information, assigned by CDCR based on a combination of self-reports and administrative records, into categories used by the U.S. Census Bureau (Hispanic, non-Hispanic Black, non-Hispanic White, non-Hispanic Other).³ Race or ethnic groupings were mutually exclusive.

<u>Covid-19 risk score</u>. The Covid-19 risk score was developed by CDCR to grade a resident's risk of severe outcomes following SARS-CoV-2 infection. It is an index equal to the sum of weighted indicators for 17 items identified in the scientific literature as risk factors for severe Covid-19 outcomes (see Table S1 for details). For incorporation as a covariate in models on vaccine effectiveness, we top-coded Covid-19 risk score to 2, which corresponded to residents who were aged younger than 65 years with comorbidities or those aged 65 years and older.

<u>Room type</u>. Residents are housed in rooms, discrete spaces that are at least partially enclosed by solid walls. We defined room type according to the number of residents housed in each room, dichotomizing this variable into cells (rooms with 1-2 occupants) and dormitories (rooms with 3 or more occupants).

<u>Security level</u>. CDCR rates each resident's security level from 1 (lowest) to 4 (highest), based on a multifactorial assessment of the resident's risk of misconduct; this rating influences housing placement and eligibility for activities such as visitations, recreation, and penal labor. Residents with security levels of 3 and 4 lived in celled housing.

<u>Undertesting during winter outbreak</u>. Testing is neither routine, random nor compulsory, creating potential for ascertainment bias, and undetected prior infection is a source of unobserved confounding. We dichotomized testing frequency during the winter outbreak based on the number of tests each resident underwent between October 15, 2020 and March 1, 2021. Undertesting was defined as having fewer than 4 tests, which corresponds to the bottom quartile of testing during the winter outbreak among those in the study cohort. Given that residents who were admitted to SCC in 2021 would have had limited opportunity for tests during the winter outbreak, these residents were all categorized as *not undertested* irrespective of individual testing counts.

<u>Facility.</u> CDCR recorded the location of residents at the end of each day. Location information can be used to generate variables at different levels of granularity. The largest unit of observation was prison, followed by facility, building, floor, and room. For the purposes of our analysis, we fixed the value of facility relative to the first potential exposure.

<u>Housing unit.</u> Housing units are discrete cohorts within prisons, consisting of residents who co-participate in activities (e.g., recreation, laundry, dining). Housing units are typically defined at building-level, although may refer to floors or large dormitories.

Table S2 presents the characteristics of the study cohort, stratified by vaccination status and prior infection status.

1.5 Covid-19 outcomes and vaccination

The data included information about Covid-19 vaccination, testing, hospitalizations, and deaths at the person-day record level.

<u>Vaccination</u>. Prison healthcare staff recorded each dose offer, to whom it was made, and whether it was accepted or declined; this information was then entered into the CDCR electronic health record system. Residents who accepted a dose were vaccinated on the spot. Cumulative vaccination of study cohort members, by dose, is shown in Figure S4.

<u>Confirmed infection</u>. A confirmed infection was defined as a positive real-time PCR or antigen diagnostic test for SARS-CoV-2. Positive tests were assigned to the date of specimen collection. Over the study period 89% of tests were by PCR, 9% by antigen and 2% test type not reported.

³ U.S. Census Bureau. 2010 Census Summary File 1— Technical Documentation. Washington, DC: U.S. Department of Commerce. SF1/10-4 (RV).

<u>Symptomatic infection</u>. We defined symptomatic infection as confirmed SARS-CoV-2 infection with symptoms observed by CDCR healthcare staff, or objective signs of fever (≥37.8°C) or hypoxemia (SpO₂<94%) within three days prior to or 10 days after an infection was initially confirmed.

<u>Hospitalization</u>. We defined hospitalization related to a SARS-CoV-2 infection as a hospitalization that occurred within three days prior to or 14 days after initial confirmation of an infection that included Covid-19 symptoms.

2 Statistical analysis

2.1 Matching methods

Propensity score matching

In the main analysis, vaccinated and unvaccinated residents were matched on propensity scores based on the following variables:

- Prior SARS-CoV-2 infection (binary) [exact matching]
- Age (continuous)
- Race or ethnic group (Hispanic, non-Hispanic Black, non-Hispanic White, non-Hispanic Other) [exact matching]
- Covid-19 risk score (categorical: $0, 1, \ge 2$)
- Room type (cell, dorm)
- Security level (categorical: 1, 2, 3, 4)
- Undertesting during winter outbreak (dichotomous)

Nearest neighbor propensity score matching⁴ with replacement was used to match fully vaccinated residents with unvaccinated controls in a 1:1 ratio. For variables marked as "exact matching," propensity score matching was undertaken within strata defined by unique combinations of those variables.

Coarsened exact matching

We conducted a sensitivity analysis in which we used coarsened exact matching⁵ as an alternative to propensity score matching. We included a limited subset of demographic and medical characteristics that were previously identified as predictive of vaccine acceptance among incarcerated people.⁶

The following variables were used for the coarsened exact matching approach:

- Age (18-29 years, 30-39 years, 40-59 years, >60 years)
- Race or ethnic group (Hispanic, non-Hispanic Black, non-Hispanic White, non-Hispanic Other)
- Covid-19 risk score $(0, 1, \ge 2)$

Covariate balance after matching was evaluated based on mean differences between variable values (standardized for continuous variables) for the vaccinated and unvaccinated groups, with a difference of 0.2 or less considered to be acceptable (Figure S5).

2.2 Additional analytic details

Vaccine effectiveness was estimated as 1 minus the risk ratio; estimates were adjusted for the facility of residence. Cluster-robust standard errors⁸ were calculated to account for both the matching weights and pair membership for

⁴ Ho DE, Imai K, King G, Stuart EA. MatchIt: nonparametric preprocessing for parametric causal inference. J Stat Soft. 2011;42(8):1-28.

⁵ Iacus SM, King G, Porro G. Causal inference without balance checking: coarsened exact matching. Polit anal. 2012;20(1):1–24.

⁶ Chin ET, Leidner D, Ryckman T, Liu VE, Prince L. Algrid-Escudero E, et al. Covid-19 vaccine acceptance in California state.

⁶ Chin ET, Leidner D, Ryckman T, Liu YE, Prince L, Alarid-Escudero F, et al. Covid-19 vaccine acceptance in California state prisons. N Eng J Med. 2021 Jul 22;385(4):374–6.

⁷ Harder VS, Stuart EA, Anthony JC. Propensity score techniques and the assessment of measured covariate balance to test causal associations in psychological research. Psychol Methods 2010;15:234-249.

⁸ Zeileis A. Econometric computing with HC and HAC covariance matrix estimators. J Stat Soft. 2004;11(10):1-17.

propensity score matching with replacement. Bias-corrected accelerated bootstrap confidence intervals were calculated for coarsened exact matching.

In a secondary analysis, we stratified the main cohort by whether members had a prior confirmed infection. In an additional sensitivity analysis, we restricted the cohort to residents who were tested at least once during the study period.

Analyses were performed using R software, version 3.5.2 (R Foundation for Statistical Computing).

3 Ethics approval

The study was approved by the institutional review board (IRB) at Stanford University (protocol #55835). The IRB approval of the study included a waiver of consent, on the basis that CDCR provided the Stanford research team with a limited data set without direct identifiers, the data had been collected for operational purposes, and the study could not practicably be carried out otherwise.

4 Supplementary results

Vaccine effectiveness against confirmed infection was 49.5% (95% confidence interval, 31.5% to 62.7%) among those without prior confirmed infection and 80.5% (52.8% to 92.0%) among those with prior confirmed infection (Table S3).

In a sensitivity analysis using coarsened exact matching as an alternative to the main analysis using propensity score matching, estimated vaccine effectiveness against any infection was 57.6% (34.2% to 72.8%) and estimated effectiveness against symptomatic infection was 84.9% (60.0% to 96.3%).

In a sensitivity analysis restricting the cohort to those receiving at least one test during the study period (95% of the full cohort), estimated vaccine effectiveness against any infection was 59.7% (46.6% to 69.6%) and estimated effectiveness against symptomatic infection was 88.0% (68.1% to 95.5%).

⁹ Abadie A, Imbens GW. On the failure of the bootstrap for matching estimators. Econometrica 2008;76(6):1537-57.

¹⁰ Austin PC, Small DS. The use of bootstrapping when using propensity-score matching without replacement: a simulation study. Stat Med. 2014;33(24):4306–19.

5 Supplementary tables and figures

Table S1. Covid-19 risk score components and weights

Condition	Definition	Weighted Score
Age 65+	Chronologic age of 65 years or above	4
Advanced liver disease	Advanced liver disease (cirrhosis/end stage liver disease)	2
Asthma	Persistent asthma (moderate or severe) as defined by the California Correctional Health Care Services (CCHCS) asthma condition specifications	1
Cancer	High risk cancer as defined by the CCHCS cancer condition specifications (excludes most diagnoses of skin cancer and "personal history of" cancers")	2
Chronic Kidney Disease	Chronic kidney disease as defined by the CCHCS chronic kidney disease condition specifications	1
Advanced Chronic Kidney Disease/Renal Failure	Chronic kidney disease (Stage 5) as defined by the CCHCS Chronic Kidney Disease Condition Specifications OR currently receiving Hemodialysis	1
Chronic Lung Disease (other)	Cystic fibrosis, pneumoconiosis, or pulmonary fibrosis	1
COPD	Chronic obstructive pulmonary disease	2
Diabetes	Diabetes	1
Diabetes (high risk)	High risk diabetes as defined by the CCHCS diabetes condition specifications	1
Heart Disease	Any of the following cardiovascular disease conditions: cerebrovascular, congestive heart failure, congenital heart disease, ischemic heart disease, peripheral vascular disease, thromboembolic disease, valvular disease, and cardiovascular disease (not otherwise specified).	1
Heart Disease (high risk)	High risk heart disease as defined by CCHCS condition specifications	1
Hemoglobin Disorder	Hemoglobin disorders as defined by CCHCS Condition Specifications for Hemoglobinopathy, including sickle cell disorder.	1
HIV	HIV	1
HIV (poorly controlled)	HIV with a CD4 count < 200	1
Hypertension	Hypertension as defined by the CCHCS Hypertension Condition Specifications	1
Immunocompromised	Any of the following conditions: aplastic anemia, histiocytosis, immunosuppressed, organ transplant, other transplant	2
Neurologic conditions	Dementia, Parkinson's disease, multiple sclerosis, myasthenia gravis, or neurologic disorder as defined by CCHCS Condition Specifications	1
Obesity	Body mass index of 30 or above	1
Other high risk chronic condition	Any of the following conditions when they are high risk per CCHCS condition specifications: coccidioidomycosis, connective tissue disorder, endocrine disorder, or vasculitis	1
Pregnant	Pregnant	1

Table S2. Characteristics of the study cohort of incarcerated people in SCC

Demographic, health, and carceral characteristics of the study cohort. Persons within the study cohort were incarcerated in SCC on July 16, 2021 and had a close exposure to a confirmed case.

	Unvaccinated ((n=359; 43%)	Vaccinated (n=468; 57%)		
	No prior confirmed infections (n=241; 67%)	Prior confirmed infection (n=118; 33%)	No prior confirmed infections (n=291; 62%)	Prior confirmed infection (n=177; 38%)	
COVID-19 indicators					
Number of tests* - mean (sd)	3.0 (1.7)	2.9 (2.0)	3.5 (1.6)	4.3 (1.7)	
Confirmed cases	63 (26.1%)	12 (10.2%)	41 (14.1%)	6 (3.4%)	
Demographic Characteristics					
Age - mean (sd)	33.6 (9.2)	36.3 (10.0)	39.6 (10.8)	40.1 (11.2)	
$Race/ethnicity^{\dagger}$					
Hispanic	82 (34.0%)	43 (36.4%)	114 (39.2%)	78 (44.1%)	
Black	105 (43.6%)	39 (33.1%)	70 (24.1%)	42 (23.7%)	
White	36 (14.9%)	25 (21.2%)	87 (29.9%)	41 (23.2%)	
Other	18 (7.5%)	11 (9.3%)	20 (6.9%)	16 (9.0%)	
Clinical Characteristics	, ,	· /	` ,	, ,	
Covid-19 risk score [‡] - mean (sd)	0.47 (0.78)	0.60 (1.23)	0.99 (1.47)	0.92 (1.22)	
Low (0-1)	216 (89.6%)	105 (89.0%)	227 (78.0%)	141 (79.7%)	
Medium or High (≥2)	25 (10.4%)	13 (11.0%)	64 (22.0%)	36 (20.3%)	
Any pre-existing condition§	177 (73.4%)	85 (72.0%)	243 (83.5%)	137 (77.4%)	
Carceral Characteristics					
Room type					
Cell	113 (46.9%)	30 (25.4%)	130 (44.7%)	26 (14.7%)	
Dorm	128 (53.1%)	88 (74.6%)	161 (55.3%)	151 (85.3%)	
Security level					
1	80 (33.2%)	>60 (>51.7%)	94 (32.3%)	102 (57.6%)	
2	107 (44.4%)	47 (39.8%)	116 (39.9%)	62 (35.0%)	
3 & 4	54 (22.4%)	<11 (<8.5%)	81 (27.8%)	13 (7.3%)	
Undertested during winter outbreak	35 (14.5%)	53 (44.9%)	32 (11.0%)	65 (36.7%)	

^{*}Confirmed by positive PCR or antigen tests. Mean and standard deviation among persons who did not test positive.

[†]All categories other than "Hispanic or Latino" refer to non-Hispanic ethnicity.

[‡]Based on CDCR risk score (Table S1).

[§] Refers to the set of conditions identified by the Centers for Disease Control and Prevention as risk factors for increased risk of severe COVID-19 among adults of any age, specifically: advanced liver disease, asthma, cancer, chronic kidney disease, chronic obstructive pulmonary disease, cardiovascular disease, dementia, Parkinson's, diabetes, on dialysis, hemoglobinopathy disorders, HIV, hypertension, immunocompromised, lung disease, neurologic disorders, pregnancy, vasculitis, overweight, obesity, and severe obesity.

We do not report cell sizes with 10 or fewer observations, so have replaced the counts and associated percentages for security levels 1 and 3-4 with range values.

Table S3. Secondary analysis estimates of vaccine effectiveness stratified by confirmed prior infection status

Prior confirmed infection status & Vaccination status	Total	Tested (%)	Positive (%)	Symptomatic (%)	Hospitalization (%)	Effectiveness against infection
No prior infection						
Unvaccinated	241	233 (96.7%)	63 (26.1%)	3 (9.5%)	1 (0.4%)	Ref.
Vaccinated	291	285 (97.9%)	41 (14.1%)	4 (1.4%)	0 (0%)	49.5% (31.5 to 62.7)
Prior infection						
Unvaccinated	118	96 (81.4%)	12 (10.2%)	0 (0%)	0 (0%)	Ref.
Vaccinated	177	174 (98.3%)	6 (3.4%)	0 (0%)	0 (0%)	80.5% (52.8 to 92.0)
All cohort members	827	788 (95.3%)	122 (14.8%)	27 (3.3%)	1 (0.1%)	

Figure S1. Testing and cases among study cohort

In the top panel, the daily number and percentage of residents tested and those testing positive. In the bottom panel, the daily number of residents who tested positive. Testing and case series were extended over the historical period 2.5 months before the start of the study period.

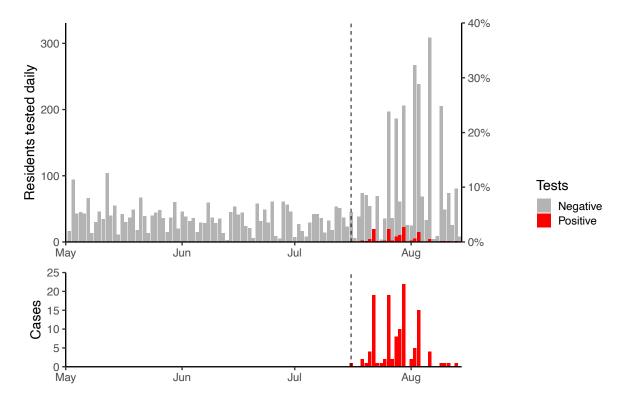


Figure S2. Cumulative number of tests by resident

Distribution across residents in counts of tests received over the study period.

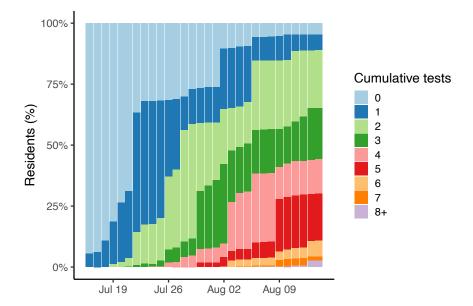


Figure S3. Distribution of prior infections among study cohort

Median time since prior confirmed infection as of July 16, 2021 was 210 days, and interquartile range was 199 to 222.

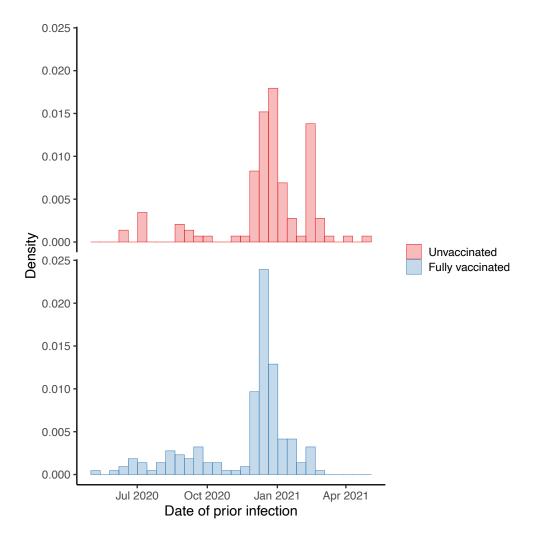


Figure S4. Cumulative vaccinations with mRNA-1273 (Moderna) among the study cohort, by dose

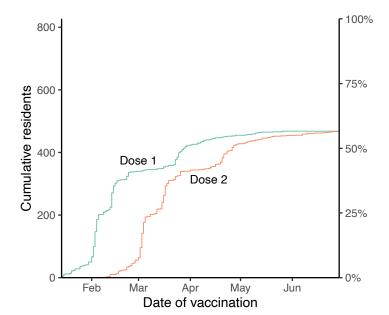
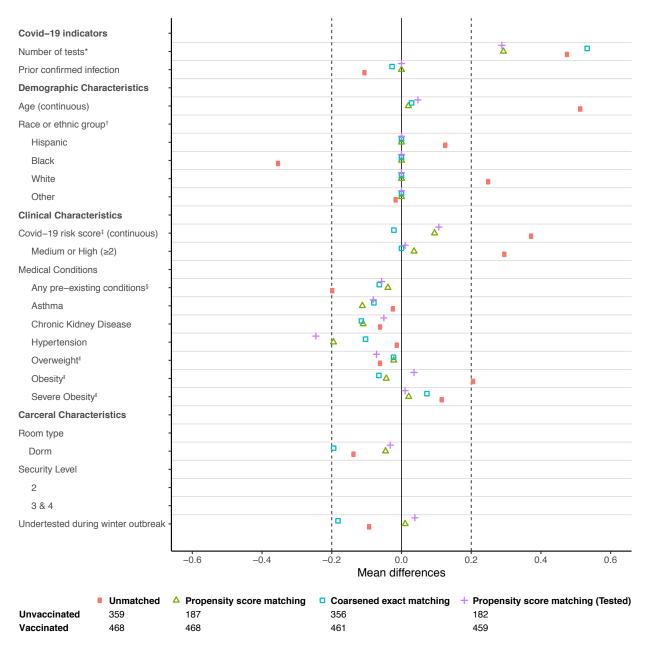


Figure S5. Covariate balance in unmatched and matched dataset, compared using standardized mean differences



^{*} Confirmed by positive PCR or antigen tests. Mean and standard deviation among persons who did not test positive.

[†] All categories other than "Hispanic or Latino" refer to non-Hispanic ethnicity.

[‡]Based on CDCR risk score (Table S1).

[§] Refers to the set of conditions identified by the Centers for Disease Control and Prevention as risk factors for increased risk of severe COVID-19 among adults of any age, specifically: advanced liver disease, asthma, cancer, chronic kidney disease, chronic obstructive pulmonary disease, cardiovascular disease, dementia, Parkinson's, diabetes, on dialysis, hemoglobinopathy disorders, HIV, hypertension, immunocompromised, lung disease, neurologic disorders, pregnancy, vasculitis, overweight, obesity, and severe obesity.

Overweight refers to 25 < BMI < 30; obesity refers to $30 \le BMI < 40$; severe obesity refers to $40 \le BMI$.